CLAIMS

1. A method for detecting a variant HBV which exhibits an altered sensitivity to an agent said method comprising:-

generating a genetic construct comprising a replication competent amount of the genome from said variant HBV contained in or fused to an amount of a baculovirus genome capable to infect cells and then infecting said cells with said construct;

contacting said cells, before, and/or during, and/or after infection, with the agent to be tested;

optionally further infecting said cells with the same genetic construct or a genetic construct comprising the genome of HBV wild-type or another HBV variant;

culturing said cells for a time and under conditions sufficient for the variant HBV to replicate, express genetic sequences and/or assemble and/or release virus or virus-like particles if resistant to said agent; and

subjecting the cells, cell lysates or culture supernatant fluid to viral- or viral-component-detection means to determine whether or not the variant virus has replicated, expressed genetic material and/or assembled and/or been released in the presence of said agent.

2. A method according to Claim 1 wherein the variant HBV is capable of replicating in the presence of an agent which inhibits or reduces infection, replication or assembly of a reference HBV.

3. A method according to Claim 2 wherein the agent is a nucleoside analogue or a non-nucleoside analogue.

4. A method according to Claim 3 wherein the agent is a non-nucleoside analogue reverse transcriptase inhibitor and/or a non-nucleoside analogue DNA dependent DNA polymerase inhibitor.

5. A method according to Claim 3 wherein the nucleoside analogue is 3TC, PMEA or PCV.

6. A method according to Claim 2 wherein the agent is an immunointeractive molecule.

7. A method according to Claim 6 wherein the immunointeractive molecule is an antibody.

8. A method according to any one of Claims 1 to 7 wherein the variant HBV comprises an altered HBV DNA polymerase.

9. A method according to Claim 7 wherein the altered HBV DNA polymerase is selected from L426I/V, L428I/VN480G, N485K, K495R, R499Q, G499E, W499Q, F512L, I515L, V519L, L526M, M550V, M550I, V553I, S565P.

10. A method according to any one of Claims 1 to 7 wherein the altered HBV is a multiple mutant selected from L526M/M550I, L526M/M550V, V519L/L526M/M550V and V519L/L526M/M550I.

11 A method according to any one of Claims 1 to 7 wherein the variant HBV comprises an altered HBV precore gene or basal core promoter.

12. A method according to Claim 11 wherein the altered HBV precore promoter or basal core promoter is selected from A1814T, C1856T, G1896A, G1897A, G1898A, G1899A, G1896A/ G1899A, A1762T/ G1764A, T1753C, G1757A and C1653T (where the numbering is from the unique *Eco*R1 site in HBV).

13. A method according to any one of Claims 1 to 7 wherein the variant HBV comprises an altered HBsAg.

14. A method according to Claim 13 wherein the altered HBsAg is selected from G112R, T123P Y/F134S, D144E, G145R, A157D, E164D, F170L, M195I, W196L, W196S, W196STOP, M198I, W199S, S204T, S210R.

15. A method according to Claim 14 wherein the altered HBsAg is selected from D144E, G145R, A157D, E164D, M195I, W196L, W196S, W196STOP, M198I, W199S and S210R.

16. A method according to any one of Claims 1 to 7 or any one of Claims 8 to 12 wherein the variant HBV comprises an altered HBV precore promoter or basal core promoter and an altered HBV DNA polymerase.

17. A method according to any one of Claims 1 to 7 or any one of Claims 11 or 12 or any one of Claims 13 to 15 wherein the variant HBV comprises an altered HBV precore promoter or basal core promoter and an altered HBV HBsAg.

18. A method according to any one of Claims 1 to 7 or any one of Claims 8 to 10 or any one of Claims 13 to 15 wherein the variant HBV comprises an altered HBV HBsAg and an altered HBV DNA polymerase.

19. A method according to any one of Claims 1 to 7 or any one of Claims 8 to 15 wherein the variant HBV comprises an altered HBV precore promoter or basal core promoter, an altered HBV HBsAg and an altered HBV DNA polymerase.

20. An HBV variant or a recombinant or derivative form thereof or a chemical equivalent thereof or a recombinant or chemical equivalent of a component thereof detected by the method according to any one of Claims 1 to 19.

21. A method according to any one of Claims 1 to 7 or any one of Claims 8 to 19 wherein the cells are co-infected with multiple combinations of the variant HBV comprises an altered HBV precore promoter or basal core promoter and/or an altered HBV HBsAg and/or an altered HBV DNA polymerase or combinations thereof.

22. A method according to any one of Claims 1 to 7 or any one of Claims 8 to 19 wherein the cells are superinfected with multiple combinations of the variant HBV comprising an altered HBV precore promoter or basal core promoter and/or an altered HBV HBsAg and/or an altered HBV DNA polymerase or combinations thereof.

23. A method for detecting a variant HBV comprising DNA polymerase which exhibits an altered sensitivity to an agent said method comprising:-

generating a genetic construct comprising a replication competent amount of the genome from said variant HBV contained in or fused to an amount of a baculovirus genome capable to infect cells and then infecting said cells with said construct;

contacting said cells, before and/or after infection, with the agent to be tested;

optionally further infecting said cells with the same genetic construct or a genetic construct comprising the genome of HBV wild-type or another HBV variant;

culturing said cells for a time and under conditions sufficient for the variant HBV to replicate, express genetic sequences and/or assemble and/or release virus or virus-like particles if resistant to said agent; and

subjecting the cells, cell lysates or culture supernatant fluid or virus purified therefrom to HBV DNA polymerase assay in the presence or absence of nucleoside

triphosphate analogues or non-nucleoside analogues reverse transcriptase inhibitors or non-nucleoside analogues DNA dependent DNA polymerase inhibitors.

24. A method for detecting DNA polymerase activity in the presence of an antiviral agent said method comprising:-

generating a genetic construct comprising a replication competent amount of a genome from an HBV capable of producing said DNA polymerase, said genome contained in or fused to an amount of a baculovirus genome capable to infect cells and then infecting said cells with said construct;

contacting said cells, before and/or after infection, with the antiviral agent to be tested;

optionally further infecting said cells with the same genetic construct or a genetic construct comprising the genome of HBV wild-type or another HBV strain;

culturing said cells for a time and under conditions sufficient for the HBV and to replicate, express genetic sequences and/or assemble and/or release virus or virus-like particles if resistant to said agent; and

subjecting the cells, cell lysates or culture supernatant fluid or virus purified therefrom to HBV DNA polymerase assay in the presence or absence of nucleoside triphosphate analogues or non-nucleoside analogues reverse transcriptase inhibitors or non-nucleoside analogues DNA dependent DNA polymerase inhibitors.